NORMAL VISION DESPITE NARROWING OF THE OPTIC CANAL IN FIBROUS DYSPLASIA

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ABSTRACT

Background Fibrous dysplasia of bone frequently involves the anterior base of the cranium and results in encasement of the optic-nerve canals. It has been assumed that such encasement leads to constriction and eventual blindness. There is controversy about whether patients should be regularly monitored or whether they should undergo prophylactic decompression of the optic nerve. This question is of particular concern in patients with normal vision, since the risks associated with surgical decompression include blindness.

Methods We studied 38 patients with fibrous dysplasia of the lesser wing of the sphenoid bone. The patients underwent a detailed neuro-ophthalmologic examination and computed tomography of the face and skull, reformatted to measure the extent of involvement of the optic canal and the area of the canals. The results were compared with those of 38 age- and sex-matched controls.

Results Of the 38 patients, 15 were male and 23 female, and their mean age was 26 years. Twelve had polyostotic fibrous dysplasia, and 26 had the McCune–Albright syndrome. Sixty-seven optic canals were affected by fibrous dysplasia; in 49 of them (73 percent) there was complete encasement. The mean (±SD) areas of the right and left canals were 9.6±3.8 mm^2 and 9.9±3.6 mm^2, respectively, in the patients, as compared with 12.0±2.9 mm^2 and 11.9±2.7 mm^2 in the controls ($P=0.009$ for the comparison of the right areas and $P=0.03$ for the comparison of the left areas by the paired t-test). In all but two of the patients, the results of neuro-ophthalmologic examination were normal. In the two patients with monocular visual impairment, the areas of the optic canals were similar on the normal and abnormal sides.

Conclusions Encasement of the optic canal in fibrous dysplasia causes narrowing of the canal, but that in itself does not result in visual loss. Therefore, prophylactic decompression of the optic nerve does not appear to be indicated on the basis of the presence of fibrous dysplasia on diagnostic images alone, since it does not correlate with visual loss. (N Engl J Med 2002;347:1670-6.)

FIBROUS dysplasia of bone is a benign condition initially described in association with skin pigmentation and endocrine dysfunction (in the McCune–Albright syndrome; number 174800 in Online Mendelian Inheritance in Man, a catalogue of inherited diseases).[1-3] In fibrous dysplasia, normal bone is replaced with fibro-osseous tissue. The fibrotic areas are composed of cells phenotypically similar to preosteogenic cells, and spicules of poorly organized woven bone are synthesized by mature but abnormal osteoblasts.[4-6]

Fibrous dysplasia is caused by a postzygotic, somatic mutation of the protein transcript of the *GNAS1* gene,[7,8] which encodes the α subunit of the stimulatory G protein. These activating mutations inhibit the intrinsic guanine triphosphatase activity of the $G_s\alpha$ protein, resulting in prolonged adenylyl cyclase activity and a subsequent increase in intracellular cyclic adenoside monophosphate.[9] Mutations at position 201 of $G_s\alpha$ in which arginine is replaced by cysteine or by histidine were found first in endocrine organs in patients with the McCune–Albright syndrome[7,8] and then in monostotic and polyostotic fibrous dysplasia and in fibrous dysplasia associated with the McCune–Albright syndrome.[10-13]

The optic nerve passes through the sphenoid wing and, in patients with polyostotic fibrous dysplasia, is often found on computed tomographic (CT) imaging to be encased by fibrous dysplasia. Clinicians may assume that such encasement will result in blindness[14-17] because of the proximity of the fibrous dysplasia to the optic nerve and because of reported cases of acute loss of vision[14,18-23] and a study that found that vision loss is the most common neurologic complication in this condition.[24]

Controversy surrounds the management of fibrous dysplasia involving encasement of the optic-nerve canals, particularly in patients whose vision is normal.[14-17,24,25] The cause of loss of vision in patients

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with fibrous dysplasia is unclear. Prophylactic decompression of the optic nerve ("unroofing") is one option[14-17,20,25]; observation with regular ophthalmologic examinations in patients with asymptomatic encasement is another. The risks associated with optic-nerve decompression include lack of improvement in vision (which is the outcome of the procedure in 5 to 33 percent of cases) and postoperative blindness.[14-17,23-25] We undertook this study to quantitate CT findings and identify any constriction of the optic canal; to determine whether there is a correlation between CT findings and the results of neuro-ophthalmologic examinations in patients with fibrous dysplasia; and, by cross-sectional analysis of a case–control cohort, to evaluate management options for patients with normal vision who have fibrous dysplasia and encased optic nerves.

METHODS

Patients

Sixty-nine patients were enrolled (in National Institutes of Health protocol 98-D-0145, entitled Screening and Natural History of Fibrous Dysplasia) between 1998 and 2001; written informed consent was obtained from each patient. To be included in the current study of optic-nerve canals, patients had to undergo a neuro-ophthalmologic examination and contemporaneous, standard CT scanning of the face and skull that showed fibrous dysplasia in the sphenoid wing. Patients were excluded from this study if they had previously undergone surgery to decompress the optic nerve, since the previous procedure and reconstruction may have resulted in distortion of the optic canal; in addition, it would have been impossible to discern whether postoperative ophthalmologic abnormalities were the result of decompression or the underlying disease. The characteristics of the patients who had undergone surgery were analyzed separately. Patients receiving bisphosphonate therapy were also excluded from the study of optic-nerve canals, since the effects of bisphosphonate treatment on fibrous dysplasia remain unclear.

Neuro-Ophthalmologic Examination

Four variables were evaluated by a neuro-ophthalmologist who was unaware of the CT findings: best corrected visual acuity, according to the Early Treatment Diabetic Retinopathy Study scale (where 20/20 denotes perfect vision); visual fields, according to Humphrey Visual Field/Swedish Interactive Thresholding Algorithm (SITA) 30-2 computerized testing (Allergan-Humphrey) or Goldmann perimetry testing; color vision, with the use of 14 Ishihara color plates; and results of examination of the fundus. There are no definitive tests for compressive optic neuropathy; therefore, abnormalities due to fibrous dysplasia were defined as either an abnormal result on the visual-field test (i.e., the presence of a scotoma or a field deficit) or an abnormal result on two of the three other tests (i.e., a visual acuity worse than 20/40, correct identification of fewer than 10 of the 14 Ishihara color plates, or evidence of optic atrophy on the fundus examination). The goal of this approach was to eliminate abnormal findings due to other causes (e.g., red–green color blindness) from consideration.

CT Imaging of the Optic-Nerve Canal

Axial CT sections were obtained through the skull base with the use of 2.50-to-3.75-mm collimation and a spiral technique (HiSpeed CTI or LightSpeed QXI, GE Medical Systems). High-resolution images of the anterior base of the skull were reconstructed at 1-to-3-mm intervals in a 20-cm field of view. The resulting volumetric data were reformatted in a double oblique plane, generating sections perpendicular to the longitudinal axis of the optic canal (Advantage Windows 3.0, GE Medical Systems) (Fig. 1). The dimensions of the optic waist were measured with digital calipers on the reformatted images; the area of the optic canal was calculated (half the height in millimeters × half the width in millimeters × π). The extent of involvement of the canal with fibrous dysplasia was assessed semiquantitatively (as 0, 25, 50, 75, or 100 percent).

Using identical acquisition and reformatting techniques, we obtained control data on age- and sex-matched patients through the National Institutes of Health Department of Radiology data base (between January and December 2001). The control patients had no history of skeletal disease and underwent routine CT imaging as part of an evaluation for sinus disease. No osseous abnormalities were seen on the CT images. A neuroradiologist who was blinded to the results of the neuro-ophthalmologic examination assessed the CT data.

Statistical Analysis

Data are presented as means ±SD unless otherwise specified. Two-sided paired t-tests were used to compare data from the patients who had fibrous dysplasia with data from the matched controls. Pearson's and Spearman's correlation coefficients were calculated to measure association. The intrarater agreement for the digital CT measurements was assessed with the use of 12 pairs of randomly chosen readings for each variable. P values of less than 0.05 were considered to indicate statistical significance. All the analyses were performed with SAS statistical software (version 6.12, SAS Institute).

RESULTS

Characteristics of the Patients

Of the 69 patients evaluated, 38 were included in the study of the optic-nerve canals. Twelve had polyostotic fibrous dysplasia, and 26 had the McCune–Albright syndrome. Fifteen of the patients were male and 23 female; their mean age was 26 years (range, 4 to 59). The mean age of the control patients was 26 years (range, 6 to 58). The age of the matched controls was within four years of the age of the study patients.

Of the 31 patients who were excluded from the study of the optic canals, 2 had irretrievable digital data (although hard copies of the CT scans showed craniofacial fibrous dysplasia, with involvement of the sphenoid wing, in 1 of the 2 patients). Ten of the excluded patients did not have fibrous dysplasia involving the sphenoid region: two had disease in the posterior skull, and eight had no craniofacial fibrous dysplasia. According to the exclusion criteria, 12 patients who were receiving bisphosphonate therapy and 7 who had undergone previous optic-nerve decompression were also excluded. The characteristics of the seven patients who had previously undergone surgery are listed in Table 1. Overall, 60 of the 69 evaluated patients (87 percent) had fibrous dysplasia that affected some area of the craniofacial region (skull, midface, or mandible).

Results of Neuro-Ophthalmologic Examination

Of the 38 study patients, only 2 had abnormal results, according to the study criteria, on neuro-oph-

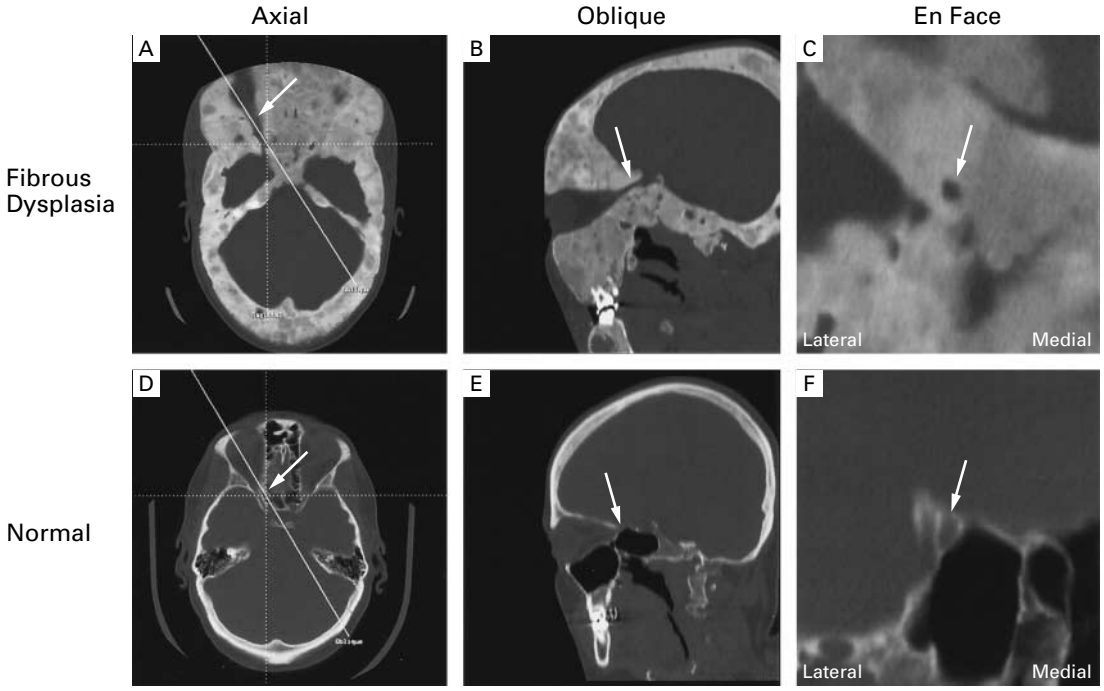

Figure 1. CT Scans of a Skull Affected by Fibrous Dysplasia and a Normal Skull.

In each panel, the arrow points to the optic nerve. Panels A, B, and C show polyostotic fibrous dysplasia involving nearly every bone in the craniofacial region. Panels A and D are axial views, with an oblique line showing the pathway of the optic canal to the optic chiasm. In Panel A, the area that appears bright is the right petrous ridge (or otic capsule), which is spared from fibrous dysplasia. Panels B and E are reformatted views along the oblique line, showing the actual pathway of the optic canal. In the fibrous dysplastic skull (Panel B), the pathway is clearly delineated because of the diseased bone; in the normal skull (Panel E), the canal is short and difficult to identify. Panels C and F are magnified views of a slice that is perpendicular to the optic canal and show the right optic canal end on (en face). Normally, the canal is oblong, as seen in the image of the normal skull (Panel F), but in the presence of complete encasement by fibrous dysplasia, the optic canal may appear round (Panel C).

thalmologic examination. In one of these two patients, visual acuity in the right eye was reduced to the ability to count fingers; because the patient was blind in the right eye, the right-eye visual fields and color vision could not be assessed; and fundus examination revealed atrophy of the right eye. All the findings in the left eye were normal. The patient had the McCune–Albright syndrome with an untreated excess of growth hormone and had lost the vision in his right eye gradually (over a five-year period). Physical examination revealed severe craniofacial deformity with substantial proptosis on the right side. The second patient with abnormal results on neuro-ophthalmologic examination had decreased color vision (9 of 14 Ishihara color plates correct) and slight pallor of the optic nerve on fundus examination on the left side; both of these variables were normal on the right side. The visual acuity was 20/16 bilaterally, with normal visual fields. Four neuro-ophthalmologic examinations over a two-year period had revealed no changes. This patient also had the McCune–Albright syndrome, with associated hyperthyroidism. Two other patients had a single abnormal neuro-ophthalmologic variable (color vision) as a result of X-linked red–green color blindness.

Of the 31 patients not included in the analysis of the optic canals, 4 had abnormal results on ophthalmologic examination; however, they had previously undergone bilateral optic-nerve decompression (Table 1). Their examination results were difficult to interpret, and it was impossible to determine whether the abnormalities were a result of underlying disease or of surgical complications. Three patients had a single abnormal variable due to amblyopia, X-linked red–green color blindness, or macular degeneration.

CT Measurements of the Optic Canal

Of the 38 study patients' optic canals, 67 canals were affected by fibrous dysplasia (Table 2). Twenty-nine of the 38 patients (76 percent) had bilateral involvement. Of the 67 involved optic canals, 49 (73 percent) were circumferentially (i.e., totally) encased with fibrous dysplasia, and 18 (27 percent) were par-

TABLE 1. CHARACTERISTICS OF THE SEVEN PATIENTS WITH CRANIOFACIAL FIBROUS DYSPLASIA WHO HAD PREVIOUSLY UNDERGONE SURGERY TO DECOMPRESS THE OPTIC NERVE.*

PATIENT	EYE	INDICATIONS FOR SURGERY	POSTOPERATIVE VISION				DIAGNOSIS
			VISUAL ACUITY†	VISUAL FIELDS	COLOR VISION‡	FUNDUS	
1	Right	Prophylaxis	20/25	Normal	14/14	Normal	Polyostotic fibrous dysplasia
2	Right	Prophylaxis	20/40	Normal	14/14	Normal	Polyostotic fibrous dysplasia
	Left	Prophylaxis	20/20	Normal	14/14	Normal	
3	Right	Gradual disturbance	20/20	Abnormal	2/14	Pallor	McCune–Albright syndrome and excess growth hormone
	Left	Prophylaxis	20/25	Abnormal	12/14	Pallor	
4	Right	Prophylaxis	Finger counting only	Abnormal	NA	Pallor	McCune–Albright syndrome, hyperthyroidism, and neonatal Cushing's syndrome
	Left	Gradual disturbance	20/40	Abnormal	7/14	Pallor	
5	Right	Gradual disturbance	20/20	Abnormal	14/14	Pallor	McCune–Albright syndrome and excess growth hormone
	Left	Acute disturbance	Finger counting only	Abnormal	NA	Pallor	
6	Right	Acute disturbance (and cyst)	20/20	Normal	Normal	Normal	McCune–Albright syndrome
7	Right	Acute disturbance (and aneurysmal bone cyst)	Finger counting only	NA	NA	Pallor	McCune–Albright syndrome and hyperthyroidism
	Left	Acute disturbance (and aneurysmal bone cyst)	Light perception only	NA	NA	Pallor	

*Patients 3, 4, 5, and 7 had abnormal results on neuro-ophthalmologic examination, but it could not be definitively determined whether the abnormalities were due to their surgery or to their underlying disease, except in Patient 4, who was newly blind in the right eye immediately after prophylactic surgery. Thus, there was postoperative vision loss in one of the five optic nerves for which prophylactic decompression was performed. All five patients with a preoperative visual disturbance had the McCune–Albright syndrome. In Patients 6 and 7, an aneurysmal bone cyst or cystic change in the area of fibrous dysplasia was also noted. NA denotes not applicable (because of blindness).

†Visual acuity was assessed according to the Early Treatment Diabetic Retinopathy Study scale, on which 20/20 denotes perfect vision.

‡Color vision was assessed according to the ability to identify 14 Ishihara color plates correctly.

TABLE 2. FINDINGS ON COMPUTED TOMOGRAPHIC EXAMINATION IN THE 38 PATIENTS WITH CRANIOFACIAL FIBROUS DYSPLASIA AND THEIR MATCHED CONTROLS.*

VARIABLE	PATIENTS WITH FIBROUS DYSPLASIA (N=38)	CONTROLS (N=38)	DIFFERENCE	P VALUE‡
No. of optic canals	67 (involved)	67 (not involved)		
Right	32	32		
Left	35	35		
Dimensions of optic canal				
Height — mm	3.7±0.9	4.2±0.6	0.48±1.2	0.001
Right	3.6±0.9	4.2±0.6	0.54±1.2	0.015
Left	3.8±0.9	4.2±0.6	0.42±1.2	0.04
Width — mm	3.3±0.7	3.6±0.5	0.29±0.9	0.007
Right	3.3±0.7	3.6±0.6	0.34±0.9	0.04
Left	3.3±0.7	3.6±0.5	0.26±0.8	0.08
Area — mm^2	9.8±3.7	11.9±2.8	2.09±4.8	<0.001
Right	9.6±3.8	12.0±2.9	2.37±4.8	0.009
Left	9.9±3.6	11.9±2.7	1.83±4.9	0.03
Extent of involvement — no.†				
Circumferential	49	NA		
Partial	18	NA		
Length of optic nerve — mm				
Right	58.4±10.2			
Left	57.7±9.1			
Difference between right and left	3.2±2.2			<0.001

*Plus–minus values are means ±SD. NA denotes not applicable.

†Involvement was considered circumferential if there was 100 percent encasement of the optic canal and partial if there was 25 to 75 percent encasement.

‡P values are for the comparison between patients and their matched controls.

tially (25 to 75 percent) encased. All the canals were patent. The mean height, width, and area of the 32 involved right canals were 3.6±0.9 mm, 3.3±0.7 mm, and 9.6±3.8 mm², respectively; the corresponding values for 32 right canals in the control group were 4.2±0.6 mm, 3.6±0.6 mm, and 12.0±2.9 mm². The mean height, width, and area of the 35 involved left canals were 3.8±0.9 mm, 3.3±0.7 mm, and 9.9±3.6 mm²; respectively; the corresponding values for 35 left canals in the control group were 4.2±0.6 mm, 3.6±0.5 mm, and 11.9±2.7 mm². The height, width, and area of the involved right optic canals and the height and area of the involved left optic canals were significantly smaller (by 14.3 percent, 8.3 percent, 20.0 percent, 9.5 percent, and 16.8 percent, respectively) in the patients with fibrous dysplasia than in the age-matched controls (Table 2). The difference between the two groups in the width of the involved left optic canal was not significant (P=0.08). There was no significant difference between the study patients and their matched controls in any of the dimensions of the six right and three left uninvolved canals.

CT evaluation of the two study patients with abnormal results on neuro-ophthalmologic examination showed that both had similar right-canal and left-canal measurements, although the vision in only one eye in each patient was abnormal (Table 3). Their canal measurements were below the range of measurements in the controls, but neither had the most constricted measurements in the study group. In one of these two patients, the right optic nerve was 26.9 mm longer than the left (a difference that was >10 SD from the mean difference in nerve length in the overall group of patients with fibrous dysplasia). The mean difference between the lengths of the right and left optic nerve in that group was 3.2±2.2 mm (P<0.001) (Table 2).

Correlations and Intrarater Variability

There was a negative correlation between the extent of involvement of either optic canal and the age of the patient (Table 4). Thus, involvement of the optic canal with fibrous dysplasia was more extensive in patients younger than 30 years of age than in patients 30 or older. For example, 80 percent of the optic canals in the 22 patients younger than 30 years were completely encased by fibrous dysplasia, whereas 44 percent of the optic nerves in the 16 patients 30 years of age or older were completely encased. In addition, there was an inverse correlation between the extent of involvement and the optic-canal measurements; hence, the greater the involvement of the optic canal with fibrous dysplasia, the smaller the area of the canal.

Analysis of the intrarater agreement for the four CT measurements (height and width of the right optic canal and height and width of the left optic canal) yielded Pearson's correlation coefficients of 0.83 (P< 0.001), 0.80 (P=0.002), 0.75 (P=0.005), and 0.70 (P=0.01), respectively, and Spearman's correlation coefficients of 0.83 (P<0.001), 0.78 (P=0.003), 0.64 (P=0.03), and 0.58 (P=0.05), respectively. For only one measurement, the width of the right canal, was there a significant difference between the two readings in the mean measurement (P=0.03 by the paired t-test).

DISCUSSION

The appropriate management of fibrous dysplasia around the optic nerve in patients with normal vision is controversial. On the basis of the assumption that there is gradual constriction of the optic nerve and inevitable visual loss, most authors recommend prophylactic decompression of the optic nerve rather than observation. However, a potential postoperative complication of this procedure is blindness. The paucity

TABLE 3. FINDINGS ON COMPUTED TOMOGRAPHIC EXAMINATION IN THE TWO PATIENTS WITH CRANIOFACIAL FIBROUS DYSPLASIA AND ABNORMAL RESULTS ON NEURO-OPHTHALMOLOGIC EXAMINATION.

DIAGNOSIS	EYE	DIMENSIONS OF OPTIC CANAL			EXTENT OF INVOLVEMENT*	LENGTH OF OPTIC NERVE
		HEIGHT	WIDTH	AREA		
		mm		mm²		mm
McCune–Albright syndrome and excess growth hormone	Right†	2.8	2.9	6.38	Circumferential	101.4
	Left	3.2	2.6	6.53	Circumferential	74.5
McCune–Albright syndrome and hyperthyroidism	Right	3.1	2.2	5.36	Circumferential	69.2
	Left†	2.5	2.1	4.12	Circumferential	69.8

*Involvement was considered circumferential if there was 100 percent encasement of the optic canal and partial if there was 25 to 75 percent encasement.

†The results of neuro-ophthalmologic examination were abnormal in this eye.

TABLE 4. CORRELATION ANALYSIS.

VARIABLE AND CORRELATION	PEARSON'S TEST		SPEARMAN'S TEST	
	CORRELATION COEFFICIENT	P VALUE	CORRELATION COEFFICIENT	P VALUE
Right optic canal				
Extent of involvement and age of patient	−0.34	0.04	−0.25	0.13
Extent of involvement and area of canal	−0.39	0.03	−0.35	0.05
Left optic canal				
Extent of involvement and age of patient	−0.41	0.01	−0.36	0.03
Extent of involvement and area of canal	−0.53	0.001	−0.52	0.001

of quantitative and long-term studies of this bone disease has made decisions about patient care difficult. The current cross-sectional study of a large, case–control cohort included comprehensive neuro-ophthalmologic examinations and analyzed diseased optic-nerve canals quantitatively with the use of CT to determine whether prophylactic optic-nerve decompression is indicated in patients whose canals are encased by fibrous dysplasia.

Statistically significant narrowing of the encased optic canal was observed in the patients with fibrous dysplasia, as compared with the controls. However, despite the constriction, 95 percent of the patients had normal results on their eye examinations. CT findings of encasement or constriction of the optic canal were not correlated with the results of the neuro-ophthalmologic examination, since all but two examinations showed no abnormalities. Therefore, we believe that fibrous dysplasia should be managed according to the results of the clinical examination and that diagnostic imaging and regular observation in these patients are appropriate. Prophylactic decompression of the optic nerve cannot be recommended on the basis of diagnostic imaging alone, since the results of such imaging do not correlate with loss of vision.

Among the patients in this study, there was a high incidence of craniofacial fibrous dysplasia in association with polyostotic fibrous dysplasia or the McCune–Albright syndrome. Sixty of the 69 evaluated patients (87 percent) had involvement of the craniofacial region, and 58 of those 60 patients had involvement of the anterior base of the cranium. The sensitivity of CT imaging allowed the detection of fibrous dysplasia in areas that would have been difficult to assess with plain radiography because of the superimposition of cranial structures.

In a study of 50 patients with cranial fibrous dysplasia, Sassin and Rosenberg reported that 10 had radiographic evidence of involvement of the optic canal and that 8 of these 10 patients had visual disturbances attributable to the surrounding fibrous dysplasia.[24] Their study was based on the use of plain radiography of the head and probably underestimated the number of encased optic-nerve canals in the patients with normal vision. In addition, the visual disturbances that were attributed to fibrous dysplasia were based on tests of visual acuity, with or without abnormal results on a fundus examination, which is a nonspecific test and not the sole measurement used to detect optic neuropathy, such as that caused by compressive, inflammatory, or demyelinating conditions.[26] Visual-field deficits and diminished color vision are sensitive but not specific indicators of compressive optic neuropathy, and diminished visual acuity and optic-nerve atrophy on a fundus examination are late findings. Changes in visual acuity, however, result in the greatest functional loss for patients. Consequently, all four variables must be considered before optic neuropathy due to compression can be diagnosed.

The proponents of prophylactic surgery believe that fibrous dysplasia is progressive, but the course of the disease is unknown. In the cross-sectional analysis of the current well-distributed cohort, 80 percent of the optic canals in the 22 patients younger than 30 years were completely encased by fibrous dysplasia, whereas 44 percent of the optic nerves in the 16 patients 30 or older were completely encased. This difference suggests that fibrous dysplasia is not progressive in the region of the optic nerve. Although regression may explain this finding, it cannot be confirmed without long-term studies of this patient population.

The cause of both the acute and gradual loss of vision associated with fibrous dysplasia remains unclear. Possible causes include optic-nerve compression by fibrous dysplasia, optic-nerve traction, and trauma to or hemorrhage into the canal. In a review, Michael et al. found that cystic masses associated with fibrous dysplasia, rather than progressive optic-canal stenosis, were frequently the cause of acute blindness.[23] In such cases, decompression of the optic nerve would not improve vision, and treatment would include resection of the imposing cyst.

In our patient with severe craniofacial deformity, uncontrolled excess of growth hormone, and gradual vision loss, the cause was believed to be traction or elongation of the right optic nerve as a result of proptosis. The degree of constriction and involvement was nearly identical in both eyes, but the right optic nerve was 26.9 mm longer than the left. Optic-nerve decompression would not have corrected this problem. The other patient with abnormal results on neuro-ophthalmologic examination had decreased color vision and slight pallor of the left optic nerve, but these findings were subtle and were stable over a two-year period, and the patient did not have functional loss of

vision or other symptoms. Thus, the abnormal findings in this patient did not confirm the presence of compressive optic neuropathy, and decompression would not have improved the patient's vision. In both of these patients, only one eye had a visual disturbance, even though both eyes had the same degree of disease involvement and even though canal measurements were similar on the left and right sides.

Visual disturbances do occur in some patients with fibrous dysplasia of the anterior base of the cranium. Of the seven patients with fibrous dysplasia who had previously undergone optic-nerve decompression, two had an associated cystic change or an aneurysmal bone cyst adjacent to the optic canal, with acute changes in vision; three had excess growth hormone or hyperthyroidism, with a gradual disturbance in vision; and all five had the McCune–Albright syndrome. The remaining two patients, who had normal vision preoperatively and underwent optic-nerve decompression for prophylaxis, had polyostotic fibrous dysplasia without endocrinopathy. Thus, 7 of the 69 patients overall (5 of those who had undergone surgery and 2 of the 38 in the study group; 10 percent) had changes in vision in the presence of the disease. However, all seven had the McCune–Albright syndrome with hyperfunctioning endocrinopathies or cystic changes in the area of the fibrous dysplasia. The effect of endocrinopathy on fibrous dysplasia and the pathologic changes (such as an expanding cyst) that convert this benign condition into an aggressive lesion will require further evaluation. Such research will help determine the predictors of visual impairment and make possible the development of effective medical and surgical therapies.

REFERENCES

1. McCune DJ. Osteitis fibrosa cystica: the case of a nine year old girl who also exhibits precocious puberty, multiple pigmentation of the skin and hyperthyroidism. Am J Dis Child 1936;52:743-7.

2. Albright F, Butler AM, Hampton AO, Smith P. Syndrome characterized by osteitis fibrosa disseminata, areas of pigmentation and endocrine dysfunction, with precocious puberty in females: report of five cases. N Engl J Med 1937;216:727-46.

3. Lichtenstein L, Jaffe HL. Fibrous dysplasia of bone: a condition affecting one, several or many bones, the graver cases of which may present abnormal pigmentation of skin, premature sexual development, hyperthyroidism, or still other extraskeletal abnormalities. Arch Pathol 1942;33:777-816.

4. Riminucci M, Fisher LW, Shenker A, Spiegel AM, Bianco P, Gehron Robey P. Fibrous dysplasia of bone in the McCune-Albright syndrome: abnormalities of bone formation. Am J Pathol 1997;151:1587-600.

5. Dorfman HD, Czerniak B. Fibroosseous lesions. In: Dorfman HD, Czerniak B, eds. Bone tumors. St. Louis: Mosby, 1998:441-91.

6. Riminucci M, Liu B, Corsi A, Shenker A, Spiegel AM, Robey PG, Bianco P. The histopathology of fibrous dysplasia of bone in patients with activating mutations of the Gs α gene: site-specific patterns and recurrent histological hallmarks. J Pathol 1999;187:249-58.

7. Weinstein LS, Shenker A, Gejman PV, Merino MJ, Friedman E, Spiegel AM. Activating mutations of the stimulatory G protein in the McCune–Albright syndrome. N Engl J Med 1991;325:1688-95.

8. Schwindinger WF, Francomano CA, Levine MA. Identification of a mutation in the gene encoding the alpha subunit of the stimulatory G protein of adenylyl cyclase in McCune-Albright syndrome. Proc Natl Acad Sci U S A 1992;89:5152-6.

9. Spiegel AM. Inborn errors of signal transduction: mutations in G proteins and G protein-coupled receptors as a cause of disease. J Inherit Metab Dis 1997;20:113-21.

10. Shenker A, Weinstein LS, Sweet DE, Spiegel AM. An activating Gs alpha mutation is present in fibrous dysplasia of bone in the McCune-Albright syndrome. J Clin Endocrinol Metab 1994;79:750-5.

11. Alman BA, Greel DA, Wolfe HJ. Activating mutations of Gs protein in monostotic fibrous lesions of bone. J Orthop Res 1996;14:311-5.

12. Marie PJ, de Pollak C, Chanson P, Lomri A. Increased proliferation of osteoblastic cells expressing the activating Gs alpha mutation in monostotic and polyostotic fibrous dysplasia. Am J Pathol 1997;150:1059-69.

13. Bianco P, Riminucci M, Majolagbe A. Mutations of the *GNAS1* gene, stromal cell dysfunction, and osteomalacic changes in non-McCune-Albright fibrous dysplasia of bone. J Bone Miner Res 2000;15:120-8.

14. Chen Y, Breidahl A, Chang CN. Optic nerve decompression in fibrous dysplasia: indications, efficacy, and safety. Plast Reconstr Surg 1997;99:22-30.

15. Moore AT, Buncic JR, Munro IR. Fibrous dysplasia of the orbit in childhood: clinical features and management. Ophthalmology 1985;92:12-20.

16. Papay FA, Morales L Jr, Flaharty P, et al. Optic nerve decompression in cranial base fibrous dysplasia. J Craniofac Surg 1995;6:5-10.

17. Ricalde P, Horswell BB. Craniofacial fibrous dysplasia of the frontoorbital region: a case series and literature review. J Oral Maxillofac Surg 2001;59:157-68.

18. Weisman JS, Hepler RS, Vinters HV. Reversible visual loss caused by fibrous dysplasia. Am J Ophthalmol 1990;110:244-9.

19. Arroyo JG, Lessell S, Montgomery WW. Steroid-induced visual recovery in fibrous dysplasia. J Clin Neuroophthalmol 1991;11:259-61.

20. Posnick JC, Wells MD, Drake JM, Buncic JR, Armstrong D. Childhood fibrous dysplasia presenting as blindness: a skull base approach for resection and immediate reconstruction. Pediatr Neurosurg 1993;19:260-6.

21. Bocca G, de Vries J, Cruysberg JRM, Boers GHJ, Monnens LAH. Optic neuropathy in McCune-Albright syndrome: an indication for aggressive treatment. Acta Paediatr 1998;87:599-600.

22. Papadopoulos MC, Casey AT, Powell M. Craniofacial fibrous dysplasia complicated by acute, reversible visual loss: report of two cases. Br J Neurosurg 1998;12:159-61.

23. Michael CB, Lee AG, Patrinely JR, Stal S, Blacklock JB. Visual loss associated with fibrous dysplasia of the anterior skull base: case report and review of the literature. J Neurosurg 2000;92:350-4.

24. Sassin JF, Rosenberg RN. Neurological complications of fibrous dysplasia of the skull. Arch Neurol 1968;18:363-9.

25. Edelstein C, Goldberg RA, Rubino G. Unilateral blindness after ipsilateral prophylactic transcranial optic canal decompression for fibrous dysplasia. Am J Ophthalmol 1998;126:469-71.

26. Seiff SR. Optic nerve decompression in fibrous dysplasia: indications, efficacy, and safety. Plast Reconstr Surg 1997;100:1611-2.